REMARKS

Claims 1-32 are pending and under consideration. Claims 8, 16, 26, and 38, are canceled herein without prejudice or disclaimer. Claims 1, 7, 9, 15, 20, 25, 28, 31, and 32, are amended herein, as indicated in the Listing of Claims. Claim 39 to 42 have been added. After entry of the present Amendment, claims 1-7, 9-15, 17-25, 27-32, and 39-42 will be pending and under consideration.

The amendments do not require a new search or raise new issues for consideration because they merely address issues already raised by the Examiner or define Applicants' invention more clearly. The amendment to claim 1, 9, 20, 28, and 31, which recite that the detector tag is a peptoid, are supported, for example, by claims 8, 16, and 26 as filed. The amendments to claims 7, 9, 15, 25, and 32 remove claim elements and thereby do not add new matter. Newly added claims 39 to 42 are supported, for example, by paragraphs [0085] to [0087] and figures 16 and 17 of the present application as filed.

It is submitted that the amendments place the claims in condition for allowance or in better condition for appeal by reducing the number of issues for consideration on appeal. The amendments were not made earlier in the prosecution because it is maintained that the previously pending claims were allowable. Since the amendments do not add new matter or require a new search or consideration, and place the claims in condition for allowance or in better condition for appeal, entry of the amendments is respectfully requested, as well as reconsideration of the pending claims in view of the remarks and amendments herein.

Rejection Under 35 U.S.C. §103(a)

Claims 1-28, 31 and 32 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Koster et al. (U.S. Pat. No. 6,043,031) in view of Monforte et al. (U. S. Pat. No. 6,635,452). To establish a *prima facie* case of obviousness there must be some suggestion or motivation in the prior art to make the claimed invention, there must be a reasonable expectation of success, and the prior art reference must teach or suggest all of the claim limitations. MPEP §2142; In re Vaeck, 947 F.2d 488, 20 USPQ2d, 1438 (Fed. Cir. 1991).

The Office Action alleges that Koster et al. teach all of the elements of the rejected claims except de-linking a mass label for detection, which the Office Action explicitly acknowledges is not disclosed in Koster et al. However, the Office Action alleges that Monforte et al., teach methods for releasing mass labels for detection prior to spectrometric analysis. Furthermore, the Office Action alleges that it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Koster et al. to release the mass label for detection, since allegedly Monforte et al. expressly suggest that in mass spectrometric methods involving nucleic acids, it is sometimes desirable to release the mass label since the nucleic acid molecules do not always desorb well.

Claims 1, 9, 20, and 28, from which the remaining claims cited in the rejection depend, recite that the detector tag is a peptoid. Neither Koster et al. nor Monforte et al. disclose peptoid tags. The Office Action cites Koster et al. as teaching peptoid tags in its teaching of the use of oligoglycine as a mass modifier. However, this teaching discloses the use of peptides and not peptoids. As disclosed in the present specification, peptoids are structurally different than peptides (see e.g., Figure 4) and offer advantages in the methods of the pending claims, as discussed in more detail below. Monforte et al. does not provide the missing teaching or suggestion of Koster et al., because Monforte et al. are also silent regarding peptoid tags. Accordingly, the cited references either alone, or in combination, do not teach or suggest all of the claimed limitations because they do not teach or suggest the use of peptoid detector tags in the methods of the pending claims.

As discussed in the present specification, peptoids offer many advantages over other labels including peptides. For example peptoids are particularly suitable for creating combinatorial libraries of tags because they have a single repeated linking chemistry scheme, a wide variety of monomer substitutions can be chosen, and they are thermally and chemically stable (See e.g., paragraph [0049]). Furthermore, creation and manipulation of the libraries of peptoid tags are relatively easy and isotopic tags can easily be incorporated into peptoids (Id.). Finally, peptoids offer advantages over peptides in that since they are not naturally occurring, they "look" different from peptides and other naturally occurring compounds, and therefore are

more easily detected in a solution that includes naturally occurring molecules, and are biostable (Id.).

Regarding claim 18, which recites that each first oligonucleotide linked to a selector tag has a different tag, the cited references are silent with respect to this element as well. Although Koster et al. mention using a biotin labeled oligonucleotide, they are silent with respect to using a different selector tag with a different first oligonucleotide. Monforte et al. do not provide the missing teaching or suggestion of Koster et al., because Monforte et al. is silent with respect to selector tags. The ability to use different selector tags can provide a control reaction and further provides the ability to use methods of the pending claims for multiplex analysis, for which the art has had a long-felt need (Paragraph [0078] to paragraph [0079]. Accordingly, the patentability of claim 18 over the prior art is even further established by its recitation that the first oligonucleotide linked to a selector tag has a different tag.

Regarding claims 7, 15, and 25, wherein the selector tag is a fluorescent moiety, the cited art is silent with respect to this element. The Office Action alleges that Koster et al. teaches using a biotin selector tag. However, Koster et al. is silent regarding using any other type of selector tag. Monforte et al., does not provide the missing teaching because it is silent with respect to a fluorescent selector tag as well. As indicated in the present specification, the use of a fluorescent moiety allows optical sorting to be used to separate the oligonucleotides (Paragraph [0077]). The prior art is silent with respect to using a fluorescent moiety, rather than a specific binding pair member, to separate the oligonucleotide. Regarding claim 32, wherein both the detector and the selector tag is a peptoid, as indicated above, since the cited art is silent with respect to the use of peptoid tags, it is silent with respect to this element as well, and aspects wherein both the detector and the selector tag is a peptoid are even further patentable over the cited art. Accordingly, Applicants respectfully request withdrawal of the rejection of claims 1-28, 31 and 32 under 35 U.S.C. §103(a) as being unpatentable over Koster et al. (U.S. Pat. No. 6,043,031) in view of Monforte et al. (U. S. Pat. No. 6,635,452).

Claims 29 and 30 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Koster et al. (U.S. Pat. No. 6,043,031) in view of Monforte et al. (U. S. Pat. No. 6,635,452) and further in view of Kinzler et al. (U.S. Pat. No. 5,695,937). Applicants respectfully traverse the rejection. The Office Action cites the Koster et al. and Monforte et al. as discussed above, but acknowledges that Koster et al. in view of Monforte et al. do not teach alternate separation moieties such as capture using polyA tails or 5' capped nucleic acids. However, the Office Action alleges that Kinzler et al. teach using streptavidin beads to isolate the defined 3' nucleotide sequence tag when an oligo dT primer used for cDNA synthesis is biotinylated. Therefore, the Office Action concludes that Kinzler et al. teach that the 5' caps and poly-A tails captured with oligo dT primers are equivalents to biotin/streptavidin.

Claim 28, from which claims 29 and 30 depend, recites that the detector tag is a peptoid. Neither Koster et al., Monforte et al., nor Kinzler et al., singly or in combination, disclose peptoid tags. The Office Action cites Koster et al. as teaching peptoid tags in its teaching of the use of oligoglycine as a mass modifier. However, this teaching discloses the use of peptides and not peptoids. Monforte et al. does not provide the missing teaching or suggestion of Koster et al., because Monforte et al. are also silent regarding peptoid tags. Furthermore, Kinzler et al., does not provide this element because it is also silent regarding peptoid tags. Accordingly, the cited references either alone or in combination, do not teach or suggest all of the claimed limitations.

As discussed above and in the present specification, peptoids offer many advantages over other labels including peptides. For example peptoids are particularly suitable for creating combinatorial libraries of tags because they have a single repeated linking chemistry scheme, a wide variety of monomer substitutions can be chosen, and they are thermally and chemically stable (See e.g., paragraph [0049]). Furthermore, creation and manipulation of the libraries of peptoid tags are relatively easy and isotopic tags can easily be incorporated into peptoids (Id.). In addition, peptoids offer advantages over peptides in that since they are not naturally occurring, they "look" different from peptides and other naturally occurring compounds, and therefore are more easily detected in a solution that includes naturally occurring molecules, and are biostable

(Id.). Finally, oligonucleotides having peptoid detector tags are well-suited to separation based on a poly A tail or a 5'-capped nucleic acid, because peptoids do not interfere with this separation [0075]. Accordingly, Applicants respectfully request withdrawal of the rejection of claims 29 and 30 under 35 U.S.C. §103(a) as being unpatentable over Koster et al. (U.S. Pat. No. 6,043,031) in view of Monforte et al. (U. S. Pat. No. 6,635,452) and further in view of Kinzler et al. (U.S. Pat. No. 5,695,937). It is also noteworthy regarding newly added claims 39-42, that the cited references are silent with respect to using an isotopic internal standard or quantitating the detector tag relative to an isotopic internal standard.

CONCLUSION

In view of the amendments and the above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. If any additional fee is required in connection with the filing of this Response, the Commissioner is authorized to charge any fee (or credit any overpayment) to Deposit Acct. No. 50-1355.

The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application.

Respectfully submitted,

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